

Med-Tox Group

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Dr. Scott A. Masten
Office of Chemical Nomination and Selection
NIEHS/NTP
PO Box 12233
MD A3-07
Research Triangle Park, NC 27709

RE: 6/12/2002 Federal Register Request for Comments, NTP substance nominations

Dear Dr. Masten:

The plan to examine ephedra alkaloid 'dietary supplements' due to the lack of adequate toxicological information will be a complex task.

Much information is already known about ephedra alkaloid toxicology, profound building blocks of cardiovascular and autonomic pharmacology and of cardiovascular medicine and pathophysiology. This fundamental information, which can be found in virtually all medical textbooks of pharmacology and medicine, has been personified in tens of thousands of adverse reaction reports and far more un-reported clinical experiences, thousands of which have been causally assigned to ephedra alkaloids by ephedra marketers and their litigation consultants, Poison Control Centers and physicians. Hundreds of published studies demonstrate and explain ephedra alkaloid toxicity.

At least one ephedra marketer sponsored animal testing of its product, finding cardiac arrhythmia and toxic CNS stimulation at clinically relevant doses. It appears that the lethal dose of ephedra/guarana (vis a vis its ephedra alkaloid/caffeine content) is substantially less than pure ephedrine/caffeine.

NTP testing of ephedra alkaloids may be compromised by:

1. The true identity of the substance tested, and its relevance to commercial products. Even pharmaceutically prepared ephedra extracts will vary from dose to dose, batch to batch and year to year. The manufacture of currently available ephedra supplements adds substantially more confusion to product identity. For example, the largest selling ephedra supplement contains uterus, ovary and

prostate, but fails to list these likely prohibited animal parts to its label. Assuming actual ephedra from China is used in ephedra supplements, pesticides and heavy metals are likely to be present in commercial samples. Ephedra contains a quinolone antibiotic. As pointed out by a journal reviewer for a rejected ephedra clinical trial, the cardiovascular toxicity of ephedra/guarana appears greater than pharmaceutical ephedrine/caffeine. It should be noted that ephedra supplements likely contain thousands of unknown chemicals

2. Scientific literature documents that the toxicity of ephedrine is directly related to ambient temperature. An increase in a few degrees centigrade decreases LD50 to about 10% of that found at room temperature.
3. Physical activity is known to modify ephedrine pharmacokinetics and toxicity.
4. Scientific literature shows that ephedra and guarana can be genotoxic and mutagenic.

Ephedra marketers widely (but falsely) support the impossibility of adverse reactions to their products, although entirely unqualified to make such a determination, with a earlier NTP study on the drug ephedrine sulfate. Therefore, NTP must be cautious in how it presents its data at the conclusion of any further NTP testing.

Notably, ephedra supplements are largely based on a prescription drug (Letigen, DAK/Nycomed) approved only in Denmark.

Having studied ephedra alkaloids for thirty years as a research scientist and R&D executive, I am aware of no scientific, medical or nutritional basis for considering ephedra alkaloids as food supplements. My analysis of DSHEA can find no basis for considering ephedra alkaloids, particularly the manipulated ma huang extract purportedly used in ephedra supplements, as food supplements.

Ephedra alkaloids are drugs, not nutrients, not nutritional, and not a therapy for any nutritional deficiency. Ephedra supplement claims are not 'structure/function' claims pursuant to DSHEA. Rather, ephedra alkaloids (other than pseudoephedrine) and ephedra are contraindicated or banned by the the United States Marines and other military services, National Collegiate Athletics Association, International Olympics Committee, United States Football League, American Medical Association, American Obesity Association, American Dietetic Association, National Institutes of Health, National Heart Lung and Blood Institute, National Association for the Study of Obesity, Canadian health department, a national pilot association, Association of Food and Drug Officials, American Heart Association, Health Research Group and many Western and Chinese scientists and physicians. These organizations do not believe that ephedra alkaloids are safe and effective as food supplements, disease treatments or energy enhancers. Ephedrine/caffeine has been banned in the US since 1983.

Sincerely,

